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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/814,232	04/01/2004	Kei Takenaka	500.43725X00	5361
20457	7590	12/11/2007		
ANTONELLI, TERRY, STOUT & KRAUS, LLP 1300 NORTH SEVENTEENTH STREET SUITE 1800 ARLINGTON, VA 22209-3873			EXAMINER BOWERS, NATHAN ANDREW	
			ART UNIT 1797	PAPER NUMBER
			MAIL DATE 12/11/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/814,232

Applicant(s)

TAKENAKA ET AL.

Examiner

Nathan A. Bowers

Art Unit

1797

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 October 2007.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 3-11 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 3-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

- 1) Claim 9 is rejected under 35 U.S.C. 102(b) as being anticipated by Franzen (US 6180372).

Franzen discloses a nucleic acid amplifying method comprising a branch step for branching a reaction fluid containing a sample of nucleic acid and reagent. Column 8, lines 29-49 state that a flow passage includes a branch portion (Figure 2:2) that creates a plurality of parallel fluid passages (Figure 2:3). Column 6, lines 30-52 and column 8, line 29 to column 9, line 2 indicate that the branched reaction fluid parts are repeatedly heated and cooled at a plurality of different temperatures.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

2) Claims 1, 7 and 8 rejected under 35 U.S.C. 103(a) as being unpatentable over Franzen (US 6180372) in view of Fouillet (US 20060011478).

With respect to claims 1 and 7, Franzen discloses a nucleic acid amplifying apparatus comprising a flow passage through which a reaction fluid containing a nucleic acid and a reagent flows. The flow passage includes a flow passage branch portion (Figure 2:2) at which the flow passage branches into a plurality of branch flow passages (Figure 2:3). A junction portion (Figure 2:4) is also provided at which the plurality of flow passages join. This is described in column 8, line 29 to column 9, line 2. Column 6, lines 30-52 state that a heating mechanism is

provided to cycle the fluid moving through the branch flow passages through a plurality of different temperatures. Franzen, however, teaches that a heating element is used to produce different temperatures over time. Franzen does not expressly disclose a plurality of set temperature zones provided by a first and second heating mechanism.

Fouillet discloses a thermal cycling device capable of amplifying nucleic acid samples via PCR. Paragraph [0205] indicates that a flow passage (Figure 12:1) is provided such that fluids are repeatedly passed through a plurality of zones (Figure 12:4,5,6) heated by different heating mechanisms.

Franzen and Fouillet are analogous art because they are from the same field of endeavor regarding thermal cycling apparatuses.

At the time of the invention, it would have been obvious to replace the programmable heating mechanisms of Franzen with a plurality of heating elements maintained at a set temperature. In Figure 12, Fouillet teaches that it is known in the art to repeatedly move fluids across several heating areas in order to produce a temperature change in the nucleic acid solution. One of ordinary skill in the art would recognize that the use of first and second heating mechanisms maintained at steady temperatures would offer a viable and effective alternative to the use of a single heating mechanism that is cycled between two temperatures. Moving a nucleic acid sample repeatedly across a several set heating regions in order to affect temperature change in the fluid is considered to be well known in the art.

With respect to claim 8, Franzen and Fouillet disclose the combination as previously described above. In addition, Fouillet indicates in paragraph [0128] that it is known to provide microfluidic thermal cycling devices with an integrated detection system capable of detecting a

desired product. At the time of the invention, it would have been obvious to ensure that the system of Franzen is provided with a detection part that detects the nucleic acid in the reaction fluid following and/or during thermal cycling. In this way, the use of additional, remote detection devices would no longer be necessary, which would improve the efficiency of the operation.

3) Claims 3-6, 10 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Franzen (US 6180372) in view of Fouillet (US 20060011478) and Enzelberger (US 20050221373).

Franzen and Fouillet disclose the combination as previously described in the rejections above, however do not expressly disclose that the use of a second branch portion and second branch flow passages.

Enzelberger discloses a microfluidic system in which a plurality of flow passages (Figure 5:S1-S5) containing a nucleic acid solution are repeatedly split and recombined to form a grid of discrete temperature areas (Figure 5:502). This is disclosed in paragraphs [0113]-[0121]. Each temperature area represents a junction portion that produces branch flow passages. Figure 5 indicates that a plurality of junction portions are provided in order to provide thermal cycling during PCR. A plurality of additional flow passages (Figure 5:P1-P5) are capable of delivering reagents to the reaction areas.

Franzen, Fouillet and Enzelberger are analogous art because they are from the same field of endeavor regarding microfluidic thermal cycling devices.

At the time of the invention, it would have been obvious to alter the apparatus and method set forth by Franzen and Fouillet in order to provide a second branch portion and second branch flow passages disposed downstream from the first branch portion and the first branch flow passages. Enzelberger teaches that microfluidic devices comprising multiple branching steps are well known in art. The addition of a second branch portion to Franzen's device would have been beneficial because it would have allowed the sample solution to experience extra temperature cycles capable of enhancing nucleic acid amplification. Since Franzen already discloses the use of a branch portion and branch flow passages subjected to heating, the addition of a second branch portion and second branch flow passages merely represents the duplication of parts already disclosed in the prior art. It would have been apparent to add second, third, fourth, etc branch portions to the system of Franzen to obtain the expected result of additional thermal cycling area. See MPEP 2144.04.

Response to Arguments

Applicant's arguments filed with respect to the 35 U.S.C. 102 rejection involving Franzen have been fully considered but they are not persuasive.

Applicant's principle arguments are

(a) In Franzen, the manner in which the heating and cooling variations are conducted differs greatly from that of the instant invention. Franzen fails to disclose a first set temperature of 95 degrees Celsius and a second set temperature in the range of 55-62 degrees Celsius.

In response to Applicant's arguments, please consider the following comments.

PCR is well known in the art to involve thermal cycling between set temperatures of 95 degrees Celsius and the range of 55-62 degrees Celsius. In column 2, lines 13-40, Franzen clearly discloses that a first set temperature at 95 degrees Celsius is used to accomplish "melting" of the DNA double helix. The same passage also clearly states that at *about* 55 degrees Celsius, primers are then attached. The term "about" implies that a range of temperatures near 55 degrees Celsius is used for this step. This range of temperatures certainly overlaps and is most likely constrained within the range set forth in Applicant's claims.

Applicant's arguments filed with respect to the 35 U.S.C. 103 rejections involving the combination of Franzen and Fouillet have been fully considered but they are not persuasive.

(a) Fouillet teaches way from an arrangement in which micro-channels are arranged such that the temperature zones occur successively. Fouillet states that the arrangement set forth in Figure 12 is sometimes undesirable, and that "a major drawback of this arrangement is that it imposes limits which are prohibitive for miniaturization, flexibility and throughput."

In response to Applicant's arguments, please consider the following comments.

While it is agreed that Fouillet cautions that there are drawbacks to implementing configuration set forth in Figure 12, Fouillet in no way states that the use of successive temperature zones regulated by separate heaters is inoperable. In fact, Fouillet indicates that this arrangement is notoriously well known in the art. It is well within the purview of one of ordinary skill in the art to weight the negative aspects of the Figure 12 design (difficulty in miniaturization) against the inherent benefits of the design (quicker thermal cycling - no need to wait while the single heater heats up and cools down during cycling). Fouillet does not

necessarily teach away from the proposed design, but rather indicates that the design is well known in the art and operates in a predictable and efficient manner.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The Fouillet (US 6680193) reference discloses the state of the art regarding microfluidic thermal cycling apparatuses that comprise a plurality of heating devices.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nathan A. Bowers whose telephone number is (571) 272-8613. The examiner can normally be reached on Monday-Friday 8 AM to 5 PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gladys Corcoran can be reached on (571) 272-1214. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



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